amended as suggested by the Examiner to fix this error.

Rejections -35 USC 112

The Examiner has rejected all claims on indefiniteness grounds from a belief that claim 1 omits essential steps of polypeptide isolation and purification.

In response, applicants point out that specific purification and isolation of polypeptide outside of binding between the detection signal and solid phase, as recited in the claims, are not required. In fact, these are surprising advantages of the claimed invention. In particular, the claims recite the detection or enrichment of antibody, without the necessity of isolating or purifying the polypeptide, which is not essential.

Step (a) recites: "the expressed polypeptide is bound to a solid phase." Step (c) recites that "the antibodies which are formed in step (b) are reacted with the polypeptide formed in step (a) and detected or enriched. The immobilized polypeptide from step (a) selectively binds to antibody. Applicants point out that the immobilization step of (a) by itself is not necessarily a purification step. Rather, the combination of immobilized polypeptide with antibody as recited in step (c) is a purification. The purification arises from the selectivity between the antibody and the immobilized polypeptide. It is not necessary to purify the antibody in step (b) prior to reacting the antibody in step (c). For example, when antibodies have been produced in rabbits by genetic immobilization according to step (b), the sera from the rabbits may be contacted with the immobilized polypeptide produced by transient transfection of cell culture cells. Purification of the antibody may be achieved in step (c), but is not required in step (b).

Because the claims as recited operate properly as described above and additional steps are not needed, the Examiner respectfully is requested to withdraw this rejection.

The Examiner has rejected claim 1 on page 4 as allegedly indefinite because of the term "the nucleic acid." The offending word "the" has been removed by amendment.

Reconsideration and allowance are requested.

The Examiner has rejected claim 1 on page 4 as allegedly indefinite because of a "purpose" recitation in this claim. Recitation of a purpose is not required in the claim and has been removed by amendment.

Reconsideration and allowance are requested in view of the amendment.

The Examiner has rejected claim 1 on page 4 as allegedly indefinite because of the Examiner's opinion that operational linkage of the signal "to the nucleic acid encoding the polypeptide" is not clear. In response, applicants note that the specification on page 2, lines 35 to 39 states that the "tag sequence is linked to the sequence encoding the polypeptide." Thus, the sequence may be linked either directly (in most cases) to the nucleic acid, but could also become linked later. To acknowledge this fact, the phrase
"that is linked to the sequence encoding the polypeptide" has been added.

Reconsideration and allowance, in view of the amendment are requested.

The Examiner has rejected claim 7 on indefiniteness grounds based on the issue of whether the recited vector is the same as the vector recited in previously. The vectors are the same for this particular dependent claim. Thus, in response, applicants have amended this claim as follows: "wherein the DNA encoding the polypeptide-~~encoding DNA~~ that ~~which~~ is introduced directly into an animal in accordance with step (b) is present in ~~a~~ the expression vector."

Reconsideration and allowance are requested in view of the amendment.

The Examiner on the top of page 5 of the office action, has rejected claims 7, 8 and 10 for alleged no antecedent basis. In response, applicants have amended the claims to remove the antecedent basis requirement.

Reconsideration and allowance in view of the amendment courteously are solicited.

The Examiner on pages 5 and 6 has rejected claim 18 on the same indefiniteness grounds as claim 1 and other grounds.

Claim18 has been cancelled without prejudice or disclaimer, mooting these rejections.

Reconsideration and allowance courteously are solicited.

Applicants reserve the right to reassert claim 18 later in a more suitable form to overcome the rejections against this claim (including the alleged prior art rejections) in a later response.

Rejections - 35 USC 102 and 103

On page 6 to page 7 claim 18 has been rejected on alleged anticipation grounds. Applicants note that the material of desirable embodiments of the claimed invention differ in composition from the cited art compositions as a necessary result of the methods used. For example, a desirable composition is the mixture of antibody - signal peptide complex on solid phase, as prepared during a late step in a described procedure. Furthermore, desirable signal peptide - antibody combinations are described that also differ. Applicants have cancelled claim 18, mooting the rejection,

while recognizing that numerous product by process embodiments are possible that are not described, either inherently or explicitly by any of the cited art.

Because claim 18 has been cancelled, reconsideration is requested.

The Examiner has rejected claims 1 to 17 on alleged obviousness grounds. Content et al (US 5,736,524) was cited as disclosing the DNA vaccination of animals. But Content et al does not teach the use of an expression vector containing a detection signal. In addition, Content et al. does not teach step (c) of claim 1. Letesson et al. does not teach genetic immunization. Letesson further does not teach to express proteins in mammalian cells. A skilled artisan has no motivation to combine these documents because the documents relate to different problems.

An unexpected result was obtained by practice of the invention. The immunization according to embodiments of the claimed invention yielded surprisingly high efficiency. This is presumably due to the presence of the tag sequence, which might increase the antigenicity of the expressed polypeptide. The results shown on page 18 of the application show the high efficacy of the immunization. This positive effect was unexpected.

Assuming for the sake of argument that it may have been known to use a vector that encodes a polypeptide that comprises a detection signal for the expression of a polypeptide in a cell culture cell, such information does not automatically imply motivation to use such a vector for genetic immunization.

Most importantly, a distinguishing and claimed feature is that the vector used in the method of claim 1 has two functions. No motivation exists to combine these two functions. One function is to express the polypeptide in a mammalian host cell (step (a)) and a second is to produce the polypeptide in an animal causing the production of antibodies in the animal (step (b)). Thus, the same polypeptide is expressed and the same vector is used for both steps (a) and (b). An important feature in this regard is

that only a single vector has to be constructed and one does not have to purify the desired polypeptide for the immunization of an animal. The only thing to be known is a nucleic acid sequence that encodes the desired polypeptide. It is not obvious to use the same plasmid for genetic immunization in an animal and for the expression of the polypeptide in mammalian cell culture cells and to then detect and/or enrich the antibodies using the immobilized polypeptide expressed in the cell culture cells.

Accordingly, the very unusual combination of elements, as claimed, provides several severely useful advantages that are not taught by any of the references. The drastic reduction of effort (only one vector, no specific purification step required) is entirely unexpected and hard to understand. In fact, the office action comments pertaining to claim 1 expressed a belief that a separate purification step must be included in order for the claimed procedure to work. As explained above, the procedure yields surprising results and appears in conflict with common assumptions in this field, and is further evidence of unobviousness. Finally, the positive effect of high immunization efficiency (page 18 of the specification) also was unexpected, further showing unobviousness.

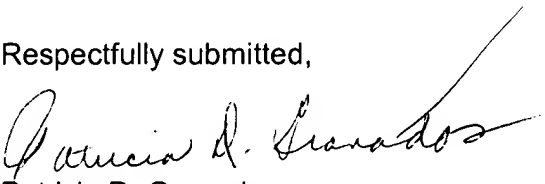
Particularly in view of the unexpected results and unorthodox procedure used (and claimed) motivation was lacking. The Examiner courteously is requested to remove the obviousness rejections and to allow the claims.

CONCLUSION

In view of the foregoing, Applicant respectfully requests the Examiner to withdraw the rejections against claims 1-14, 16-19 and 32. The Examiner is invited to contact the undersigned attorney to resolve any issues, in order to expedite the prosecution of the application.

February 7, 2003

Respectfully submitted,



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Copy of Marked-up Claims

1. A process for producing antibodies that ~~which~~ react specifically with a polypeptide, ~~wherein the nucleic acid encoding the polypeptide is known,~~ wherein:

(a) ~~the~~ DNA encoding the polypeptide is expressed in a host cell which is derived from a mammal using a vector that ~~which~~ possesses at least one sequence encoding a detection signal that is linked to the sequence encoding the polypeptide, and the expressed polypeptide is bound to a solid phase with the aid of the detection signal,

(b) independently of step (a), the DNA encoding the polypeptide is introduced directly into an animal, resulting in expression of a polypeptide in the animal, which expression causes the formation of antibodies against the polypeptide and wherein the expression vector employed for the genetic immunization in step (b)~~, for the purpose of preparing the desired antibodies,~~ is also used *in vitro* for producing the target protein, and

(c) the antibodies which are formed in step (b) are reacted with the polypeptide formed in step (a) and detected or enriched.

3. The process according to claim 2, wherein the detection sequence is selected from the group consisting of His_{6} tag sequence, the hemoglutinin sequence of an influenza virus and the myc tag sequence.

7. The process according to claim 1, wherein the DNA encoding the polypeptide ~~encoding DNA~~ that ~~which~~ is introduced directly into an animal in accordance with step (b) is present in ~~a~~ the expression vector.

8. The process according to claim 1, wherein the DNA encoding the polypeptide ~~encoding DNA~~ is introduced into the animal in step (b) using a gene gun.

10. The process according to claim 1, wherein in step (b), a genetic adjuvant is administered in addition to the DNA encoding the polypeptide ~~encoding DNA~~.

ABSTRACT

A process is provided for producing antibodies that react specifically against a polypeptide that is encoded by a nucleic acid of a known sequence. In an embodiment the nucleic acid is expressed by a host cell via a vector having at least one sequence encoding a detection signal and the polypeptide binds to a solid phase by aid of the detection signal. DNA encoding the polypeptide may be introduced directly into an animal and cause in vivo expression, resulting in the formation of antibodies specific for the polypeptide. The formed antibodies are detected or enriched by reacting with the bound polypeptide.